Kidney International, Vol. 20 (1981), pp. 717–722

Children with urinary infection: A comparison of those with and those without vesicoureteric reflux

JEAN M. SMELLIE, I.C.S. NORMAND, and G. KATZ

University of Southampton, Southampton, and University College Hospital, and Edgeware General Hospital, London, England

Vesicoureteric reflux (VUR) is present in over one-third of the children investigated following urinary infection, and it is found in over 90% of the children with renal scarring of chronic atrophic pyelonephritis [1]. New scars have been observed to develop only when infection occurs in a urinary tract in which the vesicoureteric valve is incompetent [1, 2]. Such coarse renal scarring is one of the commonest causes of hypertension in children [3] and is present in over 25% of European children and young adults requiring dialysis or renal transplantation [4]. Apart from children with an obstruction to the outflow of urine (in whom the kidney is subjected to back pressure and is particularly vulnerable to infection), renal damage is most likely to be found among children with VUR. The early recognition of these susceptible children is obviously of the greatest importance.

It is thought that VUR is generally present from birth and that deformity of the vesicoureteric junction with gross reflux may occasionally be part of a wider spectrum of congenital malformations of the urinary tract, though an aetiological role for infection has been proposed. Reflux may occur in more than one member of a family, and there are probably several modes of inheritance [5, 6].

Reflux tends to disappear with time. This has been observed in children [7–10]; it has been deduced in adults [11]; and it has been demonstrated in nonhuman primates [12].

In general, reflux is symptomless, and clinically the presence of VUR is usually unsuspected. Occasionally, in the older child or adult, transient loin pain may accompany micturition if there is marked reflux and the bladder has been allowed to become overdistended, with resulting distension of the renal pelvis. It may be suspected if residual urine is found on a second voiding within a few minutes of the first (double micturition).

Because of the importance of early recognition of children with VUR and the lack of a noninvasive screening method for its detection, we have examined the clinical features of children presenting in hospital with urinary tract infection to determine whether there were any differences between those with and those without VUR.

Methods

Between 1955 and 1975, 744 children, 179 boys and 565 girls, aged 0 to 12 years, were seen with bacteriologically proven urinary tract infection in the Children's Department of University College Hospital, London, and were investigated with both intravenous urography (IVU) and micturating cystourethrography (MCU). They were all unwell in some way, but less than half had symptoms directly related to the urinary tract. In over half of them, personal followup has continued uninterrupted since their first presentation.

All children received 7 to 10 days of an appropriate antibacterial drug, and 570 of them then received at least 6 months' low-dosage prophylaxis [13–16]. In the majority, either sulphafurazole, nitrofurantoin, or co-trimoxazole were used, but a small number were maintained on ampicillin or nalidixic acid. No change was made in the prophylactic drug prescribed if there was good compliance and no reinfection. In addition, children were encouraged to void regularly, frequently, and completely, and to void twice at bedtime (double micturition) if VUR or a residue was present. Constipation was corrected.

Bacteriological and clinical followup has continued trimonthly for at least one year in all these children. A limited IVU was repeated after two years if infection recurred to assess renal growth, and then serially at approximately 2-year intervals if VUR or renal scarring was present. A limited MCU was also repeated if VUR was seen initially. Standard methods were used, and all cystograms were carried out at least 2 weeks after elimination of bacteriuria.

Results

The ages of the children on presentation and their sex are shown in Tables 1 and 2. Of the children observed, 33% had VUR. No difference was found in the age of presentation or sex between children with or without reflux.

Findings on presentation

Radiologic abnormalities. Of the 498 children without VUR, 410 had radiologically normal urinary tracts; 21 had minor urethral irregularities, such as corkscrew urethra, not causing obstruction and considered to be within normal limits, and 67 (13%) had some other radiologic abnormality (Table 3). Among these, 24 (4.8%) had a partial or complete duplex kidney and ureter, and 7 had renal scarring of the chronic atrophic pyelonephritic type. In 5 of these patients the initial MCU was not carried out until the age of 13 or older so that VUR might have been present earlier; 1 of the 2 girls who presented under the

Received for publication April 13, 1981
0085-2538/81/0020-0717 $01.20

Table 1. Age on presentation of 744 children with urinary tract infection with and without vesicoureteric reflux (VUR)

Age in years	No VUR	VUR	Total
Under 1	108	37	145
1	20	15	35
2 to 4	135	75	210
5 to 8	163	86	249
9 to 12	72	33	105
Total	*498*	*246*	*744*

$\chi^2 = 6.29$ df = 4 NS

Table 2. Sex distribution of 744 children presenting with urinary tract infection with and without VUR

	No VUR	VUR	Total
Male	126	53	179
Female	372	193	565
Total	*498*	*246*	*744*

$\chi^2 = 1.27$ df = 1 NS

Table 3. Additional abnormalities of the urinary tract found on MCU and IVU in 498 children without VUR, and 246 children with VUR in a total of 744 children investigated after urinary tract infection

Abnormalities	No VUR ($N = 67$)[b]	VUR ($N = 103$)[b]
Kidney	($N = 61$)[c]	($N = 108$)[c]
Absent	6	1
Duplex	24 (1 scarred)	20 (6 scarred)
Horseshoe	2	2
Cyst	2	1
Ectopic	1	1
Hydronephrosis[a]	14	4
Renal scarring	7 (1 duplex)	76 (6 duplex)
Calculus	5	3
Bladder, ureter, and urethra	($N = 16$)[c]	($N = 6$)[c]
Ureterocoele	3	2
Vesicoureteric obstruction	4	2
Urethral obstruction	5	1
Hourglass bladder	2	
Diverticulum of bladder	2	1
Children undergoing surgery	25	18 + 34 ureteric reimplantation
Children not undergoing surgery	42	51

[a] Of these, 6 children with no VUR and 1 with VUR had a PUJ obstruction. Other causes of hydronephrosis are included in the group of bladder, ureter, and urethral abnormalities

[b] No. of children

[c] No. of kidneys

age of 5 had a large paraureteric saccule but never any demonstrable reflux. Abnormalities requiring surgical correction were present in 25 children without reflux. Hydronephrosis due to pelviureteric obstruction was more common in the children without reflux.

Of the 246 children with VUR, 143 had normal kidneys on IVU, and 103 (41.8%) had a further abnormality on IVU or MCU. Another 76 (31%) had renal scarring, 6 with duplex kidneys. Twenty-seven children (11%) had no scarring, but they had another abnormality, of which a duplex system in 14 was the most common. Thus, excluding renal scarring, 33 or 13.4% of the children with VUR had an additional urinary tract anomaly.

Of the children with reflux 8% had a duplex system compared with 4.8% of the children with no reflux. This observation is in keeping with the findings of Atwell et al [17].

The overwhelming majority (92%) of the children with renal scarring had reflux on their initial MCU. Because of the delayed MCU in some of the children seen early in the study, it is likely that VUR previously present had already resolved in 5.

Presenting clinical features. Although there was no age or sex difference between the two groups, there was a tendency for children with reflux who had established renal scarring or another abnormality to present later than those who had a normal IVU (Table 4 ; $\chi^2 = 12.1$, df 4, $P < 0.025$).

Table 5 shows the main symptoms, previous history of recurrent infection (defined as two or more bacteriologically proven urinary infections), and the centile height in these groups of children.

In children with VUR there was no significant increase over those without VUR in the proportion who presented with loin or abdominal pain, or with nonspecific or alimentary or urinary tract symptoms, but fever was a main symptom in a significantly greater proportion (Table 6).

Where there was no reflux, one third of the children with normal kidneys had fever, almost half of those with abnormal kidneys, and 6 of the 7 with scarred kidneys ($\chi^2 = 5.79$, df 1, $P < 0.025$). But only 8 of the 25 requiring surgical correction presented with fever, so that afebrile children with UTI must not be disregarded.

Of the children with VUR, 57% presented with fever, representing half of those with normal kidneys and two thirds of those with a renal abnormality ($\chi^2 = 6.75$, $P < 0.01$). Out of the 76 with both reflux and renal scarring 54 (71%) presented with fever.

Of the 355 children who were 5 years old or older when first seen with urinary infection, 135 (38%) were still bed wetters; half of those with both reflux and another urinary tract abnormality were enuretic (Table 5).

Height. There was no significant difference in height between children with and without reflux, as assessed using standard growth charts [18]. Very few children with reflux and normal kidneys were on or below the 10th centile in height, whereas 20% of those with reflux together with renal scarring or another abnormality were below the 10th centile. Nevertheless, 16% of the latter were over the 90th centile in height (Table 5).

Hypertension. Among those observed, 20 children had a sustained rise in blood pressure. In all but 2, reflux and renal scarring were also found. The 2 exceptions had extensive renal disease, 1 associated with renal stones and 1 with posterior urethral valves.

Previous history of recurrent infection. There was no difference in the proportion of those with and without reflux who had a past history of 2 or more proven urinary infections (Table 5), but among those with reflux, 46% of the children with scarred kidneys had a previous history of recurrent infection. This compared with only 19% of those with unscarred kidneys ($P <$

Table 4. Age on presentation in 744 children with urinary tract infection, 246 with and 498 without VUR on initial investigation

Age on presentation: years	Children without VUR						Children with VUR X-rays abnormal									
	IVU normal		X-rays abnormal		Total		IVU normal		Total		No scars		Scars		Total	
	N	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%	*N*	%
Under 1	94	22	14	21	108	22	28	20	9	9	2	7	7	9	37	15
1	16	4	4	6	20	4	7	5	8	8	4	15	4	6	15	6
2 to 4	113	26	22	33	135	27	44	30	31	30	9	33	22	29	75	30
5 to 8	141	33	22	33	163	33	52	36	34	33	8	30	26	34	86	35
9 to 12	67	15	5	7	72	14	12	9	21	20	4	15	17	22	33	13
Total	*431*	*100*	*67*	*100*	*498*	*100*	*143*	*100*	*103*	*100*	*27*	*100*	*76*	*100*	*236*	*100*

[a]The age distribution is shown in children whose IVU and MCU were otherwise normal or abnormal

Table 5. Main presenting symptoms, previous history of proven recurrent infection, and centile height on presentation, expressed as a percentage of the total children in each group among 744 children with urinary tract infection with and without VUR

Children	Children without VUR			Children with VUR			
	IVU and MCU normal (*N* = 431)	X-rays abnormal (*N* = 67)	Total (*N* = 498)	IVU normal (*N* = 143)	X-rays abnormal (*N* = 103)	Total (*N* = 246)	Total (*N* = 744)
Main presenting symptoms	%	%	%	%	%	%	%
Fever	33	48	35	50	67	57	42
Abdominal or loin pain	28	36	29	38	30	35	31
Enuresis aged 5 years or over	36	37	36	34	51	42	38
Past history							
≧ 2 proved UTI	29	33	26	19	40	28	27
Height							
≦ 10 centile	12	16	12	4	20	11	12
≧ 90 centile	14	19	14	14	16	15	15

0.001) (Table 7). Half (51%) of the children with VUR who had recurrent infections had renal scarring, compared with 23% of those who had less than 2 previous infections.

Bacteriology. The initial urinary pathogens cultured are summarized in Table 8. *E. coli* was found in 72% of the children with VUR and 73% of those without, though there was a wider range of infecting organisms among the children with VUR and another abnormality.

Immunology. A study of direct O antibody response to *E. coli* urinary infection in children [19] showed that a raised titre was obtained in 59% of 42 presenting infections in children with radiologic abnormalities (38 with VUR) compared with 33% of 36 episodes of infection in children with radiologically normal urinary tracts.

Course

A total of 580 children, 376 without reflux and 204 with reflux, were maintained for at least 6 months, on a regimen of low dosage prophylaxis [13–16] with regular complete voiding and bowel regulation.

In 77 children a surgical procedure was undertaken. In 25 children without reflux, this was mostly done to relieve obstruction or remove stones. Of the 52 with VUR, 34 had ureteric reimplantations (30 had VUR associated with established renal scarring). Most implantations were carried out before 1963 without a preliminary period of prophylaxis. In a further 18 children with reflux, other surgical procedures such as nephroureterectomy, relief of obstruction, or removal of calculus were carried out (Table 3).

During followup, reflux has so far stopped in just over half of those with renal scarring who were not treated surgically, in two thirds of those with duplications or other abnormalities, and in 80% of those with no renal abnormality. Children who have not had recent followup cystograms are included among the numbers with persisting reflux. The development of hypertension appeared to be related to the presence of established renal damage, irrespective of whether VUR was present or had disappeared.

Response to treatment. The pattern of response in children with urinary infection to low-dosage antibacterial prophylaxis together with regular, frequent, and complete bladder emptying and correction of constipation has already been described [15, 16]. Compliance of up to 90% can be obtained with co-trimoxazole and almost as high with nitrofurantoin.

During 1017 child-months' prophylaxis, no recurrence of infection occurred in 73 children without reflux; 6 reinfections occurred in 57 children with reflux during 1620 child-months' prophylaxis (1 per 22 child-years).

In 62 children who were followed for at least 1 year after prophylaxis was discontinued, 23 of the 53 children without reflux or obstruction had a reinfection within that time, mainly within 3 months of stopping, whereas in 9 children with reflux

Table 6. Fever as the main presenting symptom in 744 children with urinary tract infection with and without vesicoureteric reflux

Main symptom	Children without VUR	Children with VUR	Total
Fever	173	141	314
Other	325	105	430
Total	*498*	*246*	*744*

$\chi^2 = 34.4$ df = 1 $P < 0.001$

Table 7. Previous history of two or more bacteriologically proven urinary infections in relation to the presence or absence of renal scarring in 246 children with vesicoureteric reflux. With a history of recurrent infection 6 children had a renal abnormality but no renal scarring

Previous history of UTI	No renal scarring	Renal scarring	Total
2 or more	33	35	68
Less than 2	137	41	178
Total	*170*	*76*	*246*

$x^2 = 18.64$ df = 1 $P < 0.001$

that stopped spontaneously, 1 year before prophylaxis was discontinued, only 1 girl had a further infection, 2 years after stopping therapy.

Prognosis

Renal scarring and hypertension. During the study reported here, one boy without reflux developed severe hypertension in adolescence. Renal damage was associated with renal stones, which had been removed in early childhood. In 4 children with reflux and renal scarring, the blood pressure rose sufficiently during followup to require treatment. In 1 boy, this occurred 8 years after successful ureteric reimplantation.

Fresh scars. Fresh or extending scarring has been seen in our clinic in only 4 children, in each of whom, mainly for social reasons, attendance and compliance were poor. In a further 8 children exhibiting urinary tract infection and found to have reflux and renal scarring on investigation, earlier IVU films taken at the time of a previous urinary infection were obtained from other hospitals [2] and showed pairs of normal unscarred kidneys. All 12 had a history of previous urinary infection in addition to having VUR and presenting with a urinary infection when scarring was first seen.

Repeated infection of an unobstructed, nonrefluxing urinary tract did not result in renal scarring in any child attending our clinic.

Renal growth. The kidneys of children with unobstructed nonrefluxing urinary tracts appeared to grow normally, as determined by measurements of renal length on serial IVU's and related to the child's height [20], despite repeated symptomatic or symptomless reinfection [21]. Kidneys drained by ureters with all but the most severe degrees of reflux grew normally, provided the urinary tract was kept free from infection [9]. However, transient impairment of renal growth occasionally followed infection of the refluxing urinary tract, even if no focal scarring developed [26]. This association was significant.

Discussion

A number of noninvasive chemical and immunologic methods to identify vesicoureteric reflux have been studied, so far without success, though conflicting results have been obtained with measurement of plasma antibodies to Tamm-Horsfall protein. Renal concentration tests, which may reliably indicate transient functional impairment during renal infection, are not easily applied in infancy when the diagnosis of VUR is particularly important.

This study has not revealed any marked clinical differences between children with urinary infection who do or do not have VUR at the time of presentation. It is possible that some of the older children without reflux had previously had incompetent VU valves.

A significantly higher proportion of children with reflux and renal scarring presented with fever and also with a previous history of proved recurrent urinary tract infection, suggesting the importance of both infection and VUR in the establishment of scarring and indicating a continuing susceptibility of these urinary tracts to infection. Fever did not always occur, however, even when there was significant urinary tract malformation requiring correction.

The association of hypertension with renal scarring is well known [4]. Its late development some years after successful ureteric reimplantation in a boy with unilateral bipolar scarring [22] is in keeping with the experience of Wallace, Rothwell, and Williams, who reported the late development of hypertension in 12.5% of children with reflux corrected surgically at least 10 years earlier. All had renal scarring when hypertension was diagnosed [23]. This observation emphasizes the importance of recognizing young children who are at risk, in order to prevent scar formation. It also points out the importance of the followup of those with both VUR and established scarring, since neither surgical nor medical measures may prevent late hypertension once renal damage is established.

There is, understandably, little data available on the natural history of untreated children with urinary infection with or without VUR. The Oxford-Cardiff study of children with covert bacteriuria, found on screening school girls aged 5 and older, afforded an opportunity to compare the effect of short therapeutic courses of chemotherapy with the effect of no treatment [24]. Almost all the established scarring was confined to the group of girls with reflux. The few new scars that developed were seen in kidneys that were already scarred, drained by refluxing ureters, and exposed to urinary infection. No new scars developed in kidneys that were normal when bacteriuria was detected. Reflux tended to disappear spontaneously, even in children receiving no treatment.

In our study, the only new scars seen were in older boys following an infection of a urinary tract with moderately severe VUR into the associated ureter [2, 9]. Unlike Winberg et al [25], we did not observe any fresh scarring in children with recurrent urinary tract infection in the absence of VUR.

It was interesting to note an increased likelihood of further infection following cessation of treatment in the children without VUR. It might be suggested that the bladder residue formed by refluxed urine was responsible for the increased susceptibil-

Table 8. Urinary infecting organism on presentation in 744 children with urinary tract infection

Infecting organism	Children without VUR						Children with VUR					
	IVU and MCU normal		X-rays abnormal		Total		IVU normal		X-rays abnormal		Total	
	N	%	N	%	N	%	N	%	N	%	N	%
E. coli	316	73	48	72	364	73	114	80	67	65	178	72
Proteus	65	15	15	22	80	16	16	11	15	15	32	13
Other	50	12	4	6	54	11	13	9	21	20	36	15
Total	*431*	*100*	*67*	*100*	*498*	*100*	*143*	*100*	*103*	*100*	*246*	*100*

ity to infection in the group with reflux and that this tendency stopped when reflux ceased. In the children without reflux or obstruction, other mechanical faults in bladder emptying, such as infrequent, hurried, or incomplete voiding, or immunological deficiencies of the bladder mucosa, might have been responsible for the increased susceptibility to reinfection, which persisted if these faults were not corrected before prophylaxis was discontinued.

Vesicoureteric reflux is a common finding in childhood urinary tract infection but tends to disappear with time. We found no difference in children with or without VUR in the proportion with other congenital anomalies apart from duplex kidney. A higher proportion of acquired abnormalities of the urinary tract is associated with VUR than with a competent VU valve, and chronic pyelonephritic renal scarring occurs almost exclusively in association with VUR. Where reflux is not visualized in ureters draining scarred kidneys, it is a reasonable supposition that it has already stopped spontaneously.

In this study of 744 children with urinary infection, no differences in presenting symptoms were found between children with and without reflux, except that fever was more commonly the main presenting symptom in children with reflux. This higher incidence of fever and the delayed presentation and commoner history of recurrent infection of children with vesicoureteric reflux who also have renal scarring suggest that the combination of urinary infection and reflux are forerunners of renal damage.

Summary. In view of the importance of making an early diagnosis of vesicoureteric reflux (VUR), a retrospective study was made of 744 children aged 0 to 12 years seen at University College Hospital between 1955 and 1975 with proven urinary tract infection. One third had VUR. There was no significant difference in the sex or age of presentation between those with and without VUR, but fever was more often a presenting symptom in those with VUR. This difference was significant when renal scarring was also present. There was no other clear clinical difference between the two groups at the time of the presentation.

In our study 570 children were followed for at least one year, and about 200 for 10 to 20 years, so that a comparison was also possible between the associations, response to treatment, and progress of children with and without reflux. Renal scarring was found almost exclusively in children with VUR; the only 2 fresh scars observed developed in boys with moderate to severe reflux following infection. Hypertension developed only in children with renal damage, irrespective of the presence or absence of VUR. The early recognition, treatment, and investigation of infants and young children with urinary infection remains imperative.

Acknowledgments

These studies have been made possible by grants from the Medical Research Council, the National Kidney Research Fund, and U.C.H. Special Research Funds. We are grateful for help and encouragement over a 20-year followup period from the late Professor Lord Rosenheim, Dr. B.E. Schlesinger, Dr. R.E. Bonham Carter, Professor L.B. Strang, Dr. Robert Boyd, and for the collaboration of Drs. John Hodson, David Edwards, and R.N. Grüneberg. Mrs. Nina Prescod, B.Sc., Mrs. Anne Leakey, B.Sc., and Mrs. Marjorie Bedford gave technical and secretarial assistance. Our thanks also to Sister Jo March, her predecessors, and staff for untiring assistance in the clinics.

Reprint requests to Dr. J.M. Smellie, Senior Lecturer in Paediatrics, University College Hospital, Huntley Street, London, WC1E 6AU, England

References

1. Smellie JM, Normand ICS: Bacteriuria, reflux and renal scarring *Arch Dis Child* 50:581–585, 1975
2. Smellie JM, Edwards D, Hunter N, Normand ICS, Prescod N: Vesico-ureteric reflux and renal scarring, *Kidney Int* 8:S65–72, 1975
3. Gill DG, Mendes da Costa B, Cameron JS, Joseph MC, Ogg CS, Chantler C: Analysis of 100 children with severe and persistent hypertension. *Arch Dis Child* 51:951–956, 1976
4. Proceedings of the European Dialysis and Transplant Association (1978)
5. Leading Article. Vesicoureteral reflux and its familial distribution, edited by Stephen P. Lock. *Br Med J* 4:726, 1975
6. de Vargas A, Evans K, Ransley P, Rosenberg AR, Rothwell D, Sherwood T, Williams DI, Barratt TM, Carter CO: A family study of vesico-ureteric reflux. *J Med Genet* 15:85–96, 1978
7. Smellie JM: The disappearance of reflux in children with urinary tract infection during prophylactic therapy. *Proc 4th Int Congr Nephrology 1969*, vol 3, Karger, Basel, 1970, pp. 357–359
8. Reischauer H-C, Olbing H, Stroetges MW, Kuehn U: Disappearance of vesico-renal reflux on conservative treatment. *Germ Med Monthly* 14:187–189, 1969
9. Edwards D, Normand ICS, Prescod N, Smellie JM: Disappearance of vesico-ureteric reflux during long-term prophylaxis of urinary tract infection in children. *Br Med J* 2:285–288, 1977
10. Verrier-Jones ER, Meller ST, McLachlan MSF, Sussman M, Asscher AW, Mayon-White RT, Ledingham JGG, Smith JC, Fletcher EWL, Smith EH, Johnston HH, Sleight G: Treatment of bacteriuria in schoolgirls *Kidney Int* 8 (suppl):S85–S89, 1975
11. Baker R, Maxted WC, Maylath J, Shuman I: Relation of age, sex and infection to reflux: data indicating high spontaneous cure rate in paediatric patients. *J Urol* 95:27–32, 1966
12. Roberts JA, Riopelle AJ: Vesico-ureteral reflux in the primate II. Maturation of the uretero-vesical junction. *Pediatrics* 59:566–568, 1977
13. Normand ICS, Smellie JM: Prolonged maintenance chemotherapy in the management of urinary infection in childhood. *Br Med J* 1:1023–1026, 1965
14. Grüneberg RN, Smellie JM, Leakey A: Changes in the antibiotic sensitivities of faecal organisms in response to treatment in children with urinary tract infection, in *Urinary Tract Infection 2*,

edited by BRUMFITT W, ASSCHER AW, London, Oxford University Press, 1973 pp. 131–136

15. SMELLIE JM, GRÜNEBERG RN, LEAKEY A, ATKIN WS: Long-term low-dose co-trimoxazole in prophylaxis of childhood urinary tract infection: clinical aspects. *Br Med J* 2:203–206, 1976
16. SMELLIE JM, KATZ G, GRUNEBERG RN: Controlled trial of prophylactic treatment in childhood urinary tract infection. *Lancet* 2:175–178, 1978
17. ATWELL JD, COOK PL, HOWELL CJ, HYDE I, PARKER BC: Familial incidence of bifid and double ureters. *Arch Dis Chil* 49:390–393, 1974
18. TANNER JM, WHITEHOUSE RH, TAKISHAI M: Standards from birth to maturity for height, weight, height velocity and weight velocity. British Children 1965. *Arch Dis Child* 41:454–471, 1966
19. SMELLIE JM, PURSELL R, PRESCOD N, BRUMFITT W: Relationship between serum antibody titre and radiological findings in children with urinary tract infection, in *Urinary Tract Infection 2*, edited by BRUMFITT W, ASSCHER AW, London, Oxford University Press, 1973 pp. 31–38
20. HODSON CJ: Radiological diagnosis of renal involvement. Chapter 13, in *Urinary Tract Infection 1*, edited by O'GRADY F, BRUMFITT W., London, Oxford University Press, 1968, pp. 108–112
21. SMELLIE JM, NORMAND ICS: Experience of followup of children with urinary tract infection, in *Urinary Tract Infection 1*, edited by O'GRADY F, BRUMFITT W, London, Oxford University Press, 1968, pp. 123–135
22. SMELLIE JM, NORMAND ICS: Reflux nephropathy in childhood, Chapter 2, in *Reflux Nephropathy*, edited by HODSON CJ, KINCAID-SMITH P, New York, Masson Publishing Co. Inc., USA 1979 pp. 14–20
23. WALLACE DMA, ROTHWELL DL, WILLIAMS DI: The long-term followup of surgically treated vesico-ureteric reflux. *Br J Urol* 50:479–484, 1978
24. Cardiff-Oxford Bacteriuria Study Group. Sequelae of covert bacteriuria in schoolgirls—a four-year followup study. *Lancet* 1:889–893, 1978
25. WINBERG J, LARSON H, BERGSTRÖM T: Comparison of the natural history of urinary infection in children with and without vesicoureteric reflux, in *Renal Infection and Renal Scarring*, edited by KINCAID-SMITH P, FAIRLEY KF, Melbourne, Australia, Mercedes Publishing Service, 1972, pp. 293–302
26. SMELLIE JM, EDWARDS D, NORMAND ICS, PRESCOD N: Effect of vesicoureteric reflux on renal growth in children with urinary tract infection. *Arch Dis Child* 56:593–600, 1981